with survival; rates of local recurrence (LR) and regional recurrence (RR) have also been investigated in relation to LVI.

Results: See Table 1.

Table 1

LN	LVI	n	% in group	% 10 yr Survival
neg	Neg	3156	52	88.3
	Pos	550	9	76.9
1−3 pos	Neg	1540	26	75.2
	Pos	751	13	43.1
		5997		

Rate of LR was 3% at 10 years for LVI+ and 1% for LVI− (NS). The rate of RR in LN−/LVI+ patients was 3% at 10 years.

Conclusions: These figures verify in a multicentre International large data set that LVI+/LN− have the same survival as LN 1−3 positive cases; In LN+ cases LVI+ has no additional effect on prognosis.

LVI has a clear effect on prognosis of LN− cases whereas the effect of sentinel node micro metastases on survival is unconfirmed and LVI is more commonly found. Furthermore LVI+ does not give significantly higher rates of LR nor RR.

These findings suggest LVI could replace SLNB, being more accurate, easier and cheaper.

484 Poster Discussion

Presence of bone marrow micrometastasis predicts metastatic pattern and disease-free interval in breast cancer patients – results from the Collaborative Group Bone Marrow Micrometastasis

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Background: To establish the prognosis and metastatic pattern in breast cancer patients in relation to bone marrow micrometastasis (BMM), that are readily detectable at the time of first diagnosis of cancer, a large series of patients was analyzed.

Methods: Individual patient data of 9 studies, involving 4,686 patients with breast cancer, were combined to analyze 10-year survival, specifically distant disease-free survival and the site of distant metastasis. We constructed Kaplan–Meier curves and computed incidence rate ratios with 95% confidence intervals. Survival estimates were adjusted for study center. The difference in median disease-free survival interval between BMM positive and BMM negative patients was tested with the Wilcoxon rank sum test.

Results: BMM were detected in 1,432 (30.6%) patients. Median follow-up was 62 months. Overall, distant metastasis occurred in 952 (20.3%) patients. Compared to patients without BMM, patients with BMM experienced twice as often distant metastasis (32.3% vs. 15.1%, $P < 0.001$) and had significantly shorter distant disease-free survival (log rank: $P < 0.001$; IRR 2.36, CI: 2.07−2.69, P(Wald) < 0.001). Among patients with distant metastasis during follow-up, the localization of distant metastasis was visceral (48.4%), bone (30.5%) and multiple sites (21.1%), the latter being defined as simultaneous occurrence of bone and visceral metastasis. The proportion of metastasis at multiple sites was significantly higher in patients with BMM than in patients without BMM (25.8% vs. 16.7%, respectively; $P = 0.003$). For each localization of distant metastasis, the disease-free interval was significantly shorter in patients with BMM than in patients without BMM: the respective medians of distant disease-free intervals were 23 vs. 29 months for visceral metastasis ($P = 0.030$), 24 vs. 33 months for bone metastasis ($P = 0.001$), and 14 vs. 22 months for metastasis at multiple sites ($P = 0.004$). Post-relapse survival was not different between patients with BMM and patients without BMM.

Conclusions: The results provide conclusive evidence that presence of BMM predicts a poor-prognosis pattern of distant metastasis, characterized by earlier distant relapse and first distant metastasis at multiple sites. BMM at the time of first diagnosis of primary breast cancer may be used as surrogate marker of distant metastasis and implemented in treatment strategies.

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Impact of histological grade on prognosis in very young breast cancer patients: pooled analysis of four EORTC trials

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Background: Young age at time of diagnosis of breast cancer is associated with unfavorable prognosis. Current guidelines recommend the administration of adjuvant chemotherapy to patients aged 35 years or less regardless of any tumor characteristics. However, since breast cancer at a very young age is a relative rare event, evidence concerning prognostic factors within this subgroup is lacking. Therefore, the individual patient data of four early stage breast cancer EORTC trials were pooled to study prognostic factors on long term outcome in young breast cancer patients.

Material and Methods: The total dataset consisted of 9938 early breast cancer patients of which 12% was younger than 41 years. Tumor material from 549 patients aged less than 41 years at time of diagnosis was available for renewed pathological analysis. The median follow-up was 7 years.

Results: In multivariate analyses, histological grade remained the only independent prognostic factor for overall survival (Grade III versus I: hazard ratio (HR) 3.92; 95% confidence interval (CI) 1.38 to 11.16). In the subgroup of young node-negative patients who did not receive adjuvant chemotherapy, histological grade was even stronger related to a favourable prognosis (Grade III versus I: HR 8.92; 95% CI 1.17 to 68.20). This association was independent of tumor size, type of surgery and hormone receptor status. Survival rates were excellent for young node negative patients with grade I tumors: 97% at 7 year follow-up compared to 72% for grade III tumors.

Conclusion: Histological grade is a strong independent prognostic factor in young breast cancer patients. These findings support the fact that histological grade is an excellent diagnostic tool to assess disease outcome and to plan systemic treatment strategy in young breast cancer patients.

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Long-term prognostic impact of risk classifications in node-negative breast cancer – comparison between Adjuvant!, St. Gallen, and a novel risk algorithm used in the prospectively randomized Node-Negative-Breast-Cancer-3 trial (NNBC-3)

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Background: defining risk categories in node-negative breast cancer is of great importance. We developed a novel risk classification which is currently evaluated prospectively in the Node-Negative-Breast-Cancer-3 trial (NNBC-3) trial using well-established clinico-pathological criteria. We compared its prognostic utility with the web-based tool Adjuvant! and the St. Gallen risk classification 2007.

Methods: we retrospectively analyzed 410 node-negative breast cancer patients with a median follow-up of 10 years which did not receive adjuvant systemic therapy. Patients with either (I) age <35 years, (II) G III, (III) HER-2 positivity, (IV) vascular invasion, (V) progesterone receptor negativity, (VI) G II tumors >2 cm, or (VII) G I tumors >5 cm were defined as high-risk. All patients were also characterized using Adjuvant! and the established St. Gallen 2007 risk category. We analysed disease-free survival (DFS) and overall survival (OS) for each of these risk classifications.

Results: Adjuvant! and the St. Gallen guideline classified 17% and 18%, respectively, of the patients as low-risk. Use of the novel NNBC-3 algorithm enlarged the low-risk group to 37%. Only the NNBC-3 algorithm retained its prognostic significance for DFS in multivariate analysis ($p = 0.006$; HR 2.02; 95% CI 1.22−3.35). Both Adjuvant! ($p = 0.027$; HR 3.81; 95% CI 1.16−12.47) and the NNBC-3 risk classification ($p = 0.049$; HR 1.95; 95% CI 1.00−3.81) predicted OS in multivariate analysis independently.